

PATENT
674523-2028**REMARKS**

Reconsideration and withdrawal of the rejections of the application are requested in view of the amendments and remarks presented herein, which place the application into condition for allowance. These Remarks are being filed in conjunction with a Request for Continued Examination.

Claims 24, 26, 28-30, 33, 34, 36-38 and 40-43 are pending in this application. The Examiner has indicated in the Advisory Action that claims 28-30, 33, 34, 36-38 and 40-43 are rejected, but has not indicated the status of claims 24 and 26. Clarification is requested.

I. THE REJECTIONS UNDER 35 U.S.C. §103 ARE OVERCOME

Claims 28-30, 33, 34, 36-38 and 40-43 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Lisziewicz, Hope *et al.* and Riviere *et al.* The rejection is traversed.

There is no teaching in any of the references that renders the claimed invention obvious. Lisziewicz, Hope or Riviere, alone or in combination, do not teach a truly Tat- and Rev-inducible retroviral vector, where there is no basal transcription in the absence of Tat and Rev. On the other hand, the claimed invention achieves a Rev-dependent intron by the placement of splice sites that flank an RRE-containing intron, and by the splice sites being derived from different retroviruses. Neither Lisziewicz, Hope nor Riviere discloses a retroviral vector having splice sites derived from different retroviruses.

The Office Action suggests that it is within the routine skill of the ordinary artisan to choose splice sites from different retroviruses for design of a retroviral vector that is Tat and Rev inducible. This is not the case. Inefficient splicing is the mechanism by which there is no detectable expression of the NS in cells lacking Tat and Rev. Inefficient splicing is a consequence of the placement and nature of the splice sites in the retroviral vector, *i.e.* placement of the splice sites around the intron, and recognition of the splices as being derived from different retroviruses. Therefore, inefficient splicing is inherently achieved by the limitations recited in the claims, and it is this feature that distinguishes the claimed invention from the prior art. No teaching in any of the cited references suggests or provides motivation to effect inefficient splicing with a retroviral vector. Accordingly, one of ordinary skill in the art would find no teaching or motivation in Riviere, or in the other cited references, to use splice sites from different retroviruses in a retroviral vector designed to be both Tat- and Rev- inducible.

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The structure and function of the claimed retroviral vector particle must be found in the cited art, and that is not the case here. The claimed invention requires (1) that the intron is flanked by a retroviral splice donor (SD) site and a retroviral splice acceptor (SA) site derived from **different** retroviruses, (2) that the nucleotide sequence (NS) is capable of expression in Tat and Rev expressing cells, and (3) that NS expression is undetectable in cells not expressing Tat and Rev genes. The references cited in the Office Action and Advisory Action, alone or in combination, do not teach or suggest these features.

The Examiner relies on claims 1, 9 and 40 to assert that Riviere *et al.* teach splice sites derived from different viruses. To the contrary, Riviere *et al.* fail to teach the use of SD and SA sites that are derived from different retroviruses. In fact, **both sites are derived from an MLV-based retrovirus**. The entire description, as well as the Examples, supports this fact. Therefore, the claims cannot properly be interpreted to read on the claimed invention.

In addition, none of the references, alone or when combined, teaches a retroviral vector having the claimed structure and function. The claimed structure and function are distinct over the cited references in that the claimed vector exhibits inefficient splicing, as opposed to the strictly typical Rev/RRE export function. It is this inefficient splicing that makes the claimed retroviral vector truly Rev-inducible, resulting in no detectable expression of the NS.

Consequently, reconsideration and withdrawal of the rejection under Section 103 are requested.

CONCLUSION

Applicants believe that the application is in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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